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Mode d'emploi

Freeze dryer
Alpha 1-4 and 2-4 LD

Gefriertrocknungsanlagen

OPERATING MANUAL

Freeze Dryer

ALPHA 1-4 LD-2

(Best.-Nr. 101041 / 101141 / 101241)

ALPHA 2-4 LD-2

(Best.-Nr. 101042 / 101142 / 101242)

M A R T I N C H R I S T

Gefriertrocknungsanlagen GmbH

Operating Manual ALPHA 1-4 LD-2 and ALPHA 2-4 LD 2

Order Number:

Serial Number:

In case of inquiries or repair please state the above numbers.

For service please contact:

MARTIN CHRIST Gefriertrocknungsanlagen GmbH
An der unteren Söse 50, D-37520 Osterode
Tel. (05522) 5007-25, Telefax (05522) 5007-12

Preface

Dear customer,

Congratulations on purchasing a CHRIST freeze dryer.

The freeze dryer is equipped with user-friendly options which make the operation easier for you.

The newly designed ALPHA 1-4 LD-2 / ALPHA 2-4 LD-2 is a universally usable CHRIST freeze dryer for laboratories, R&D departments and scientific institutes. The well proven range of accessories allows application oriented configuration of the equipment especially for routine use. A practical and universally usable range of accessories is available for almost all applications for drying in round bottom flasks, dishes, ampoules and injection vials.

A special advantage is the user-friendly control system LD (Lyo-display), the functions of which are explained on the control panel:
- LC display showing the most important process data (temperature of ice condenser, vacuum)
- Conversion of temperature and vacuum in accordance with the vapour pressure curve above ice
- RS-232 communications interface (PC) is available as an option.

Especially worth mentioning is the possible retrofitting of a vacuum measuring sensor (type TPR 265) which only has to be plugged in at the back of the unit. This freeze dryer offers a wide range of functions for a variety of practical applications.

We thank you for your confidence and wish you a successful application of the freeze dryer.

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1 General Information

1.1 Introduction

What is freeze drying?

Freeze drying means: Extraction of water from frozen material. The drying process takes place by avoiding the liquid state through sublimation, i. e. direct conversion from ice to vapour. This happens under vacuum, when the temperature in the product is less than -10°C.

The aim of freeze drying is to obtain an easily water soluble product which will have the same characteristics as the original product after addition of water.

As the drying process takes place in frozen state at very low temperatures it is possible to dry e. g. albumen which will remain water soluble. Also most of the other chemical compounds will be qualitatively and quantitatively unchanged.

Freeze drying (lyophilisation) is also the most gentle process for preserving the biological properties of sensitive tissue and tissue components.

Through freeze drying the product, mainly of biological origin - such as tissues, tissue extracts, bacteria, vaccines and sera - is transformed into a dry product. During this process enzymatic, bacterial and chemical changes are largely avoided.

1.2 Applications

The freeze dryer **ALPHA 1-4 LD-2 / ALPHA 2-4 LD-2** is a high-performance, universal laboratory and pre-production unit for freeze drying of solid or liquid products in ampoules, bottles, glass flasks, wide-neck filter bottles or dishes. All operations necessary for freeze drying are possible inside the unit:

- Freezing
- Freeze drying
- Final drying

The freeze dryer **ALPHA 1-4 LD-2 / ALPHA 2-4 LD-2** is suitable for drying of e. g. bacteria and virus cultures, blood plasma, serum fractions, antibodies, sera, vaccines and pharmaceutical products such as chloramphenicol, streptomycin, vitamins, ferments as well as plant extracts for biochemical tests.

1.3 Technical Specifications of Freeze Dryer ALPHA 1-4 LD-2 / ALPHA 2-4 LD-2

Performance data:

Ice condenser capacity:	max. 4 kg	max. 4 kg
Ice condenser performance:	max. 4 kg/24 h	max. 4 kg/24 h
Ice condenser temperature:	Approx. -54°C	approx. –84°C
Shelf temperature when freezing inside the ice condenser chamber:	Approx. -25°C	approx. –50°C
Max. shelf surface area when drying outside the ice condenser chamber:	5x shelf surface areas	360
Max. shelf surface area when drying in injection vials (according to DIN) with sealing under vacuum or nitrogen atmosphere:	Only outside, with 4x shelf surface areas	250
Drying in round bottom flasks, e. g. each 300 ml:	24 pieces with additional chamber	

Other data:

Dimensions of the unit:	width: 390 mm height: 415 mm depth: 540 mm (incl. vacuum flange connection)	
Weight:	approx. 42 kg	approx. kg
Noise emissions according to DIN 45635	dB (A)	dB (A)
Electromagnetic compatibility according to EN 55011:	class B	

Filling quantities:

Refrigerant:	see label on the back of the unit

Connection requirements:

Electric connection:	230 V, 50 – 60 Hz (others on request) and central grounding connection

Max. power consumption:	0,92 kVA	1,84 kVA
Max. current:	4,0 A	8,0 A
Safety precaution	6,3 AT	10 AT
Max. ambient temperature	climate category SN +10°C to +32°C (higher temperatures on request)	

Equipment connections:

Vacuum connection:	small flange connection DN 25 KF (ISO 28403, DIN 2861)
Condensate drain:	hose nozzle DN 10 with 0.5 m silicon hose (D=8 x s = 2mm)

Scope of supply includes:

1 tube high-vacuum grease

1 litre vacuum pump oil (if pump is supplied)

1 operating manual and detailed technical documentation

0.5 m condensate drain hose (silicon 9 x 12 mm)

Scope of supply does not include:

- Commissioning of the unit will be carried out on request and charged at cost.
- Installation of the exhaust pipe of the vacuum pump (not necessary when using an exhaust filter).

1.4 Standards and Regulations

Please refer to the enclosed EU-Statement of Conformity.

1.5 Safety Instructions

1.5.1 CAUTION! Disconnect Mains Plug!

As current-carrying parts are accessible inside the unit the mains plug must be disconnected before the side panels are opened. For maintenance the unit must be switched off with the mains switch.

1.5.2 CAUTION! Solvents!

Acidic products or products with a high solvent concentration cannot be dried without special protective measures and devices such as e.g. a cooling trap for protection of the vacuum pump (if necessary check with our service department).

Special caution is necessary when using azides because a dangerous explosive develops in combination with copper or non-ferrous metals! It is absolutely essential to consult our company!

1.5.3 ADVICE! Cleaning and Maintenance of the Unit!

For infectious, toxic, pathogenic and radioactive substances the corresponding safety regulations must be observed.

1.5.4 WARNING! Freezing of Limbs to surfaces!

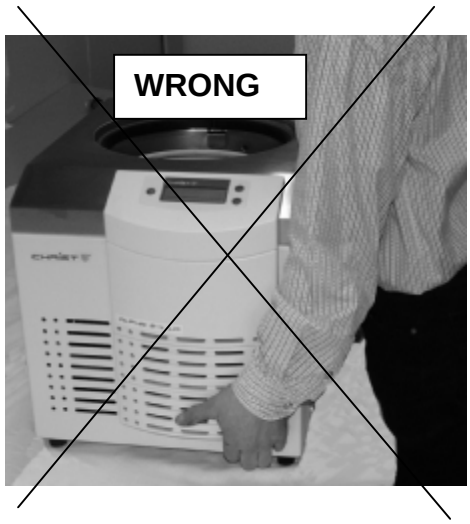
During operation of the freeze dryer dangerous situations in the ice condenser chamber may arise. When putting in the shelves take care that limbs do not come into contact with the condenser in the ice condenser chamber as the limbs may become frozen to the surface. The limb can only be detached from the surface by applying heat. Liquid should not be used.

1.5.5 IMPORTANT! Transport instructions!

Please keep the packaging for possible subsequent dispatch.

The freeze dryer should be carried by two persons by holding it underneath on both sides.

WARNING! When transporting or putting down the unit do not hold the plastic control panel. Please note: When putting the unit down on a surface there is a danger of squeezing hands or fingers.



1.6 Prohibited Freeze Drying Processes

1. Operation of freeze dryer when not installed correctly.
2. Operation without panels.
3. Operation by non-authorised personnel.
4. Operation with shelves not installed properly.
5. Operation with very corrosive substances which can cause damage to material and affect mechanical strength of chamber and shelves.
6. Operation with accessories not allowed by the manufacturer, except for commercial freeze drying vessels made of glass or plastic. The user is explicitly warned not to use poor quality goods. Breaking glass or bursting vessels can cause dangerous situations during freeze drying.
7. Operation in locations with danger of explosion.

8. During operation the freeze dryer must not be knocked or moved. Leaning against or resting on the freeze dryer is not allowed.

9. Do not place potentially dangerous material, e. g. glass vessels containing liquids, near the freeze dryer.

10. Products which could react to the supply of high energy during the freeze drying process must not be dried.

11. Do not freeze dry explosive or highly inflammable substances.

12. Substances which could damage the material of the shelves or the chamber in any way must not be dried or may only be dried when special safety measures are observed. Infectious, toxic, pathogenic and radioactive substances must only be dried in suitable vessels.

2 Installation and Commissioning of the Unit

2.1 Site of Installation

WARNING! Papers, cloths or similar items must not be put behind the unit as the air circulation of the heat exchanger will not work any more.

The freeze dryer should be positioned horizontally. The ambient temperature should be within approx. +15°C and +25°C.

The refrigerator of the freeze dryer is air-cooled. Sufficient air circulation must be ensured. A distance of at least 30 cm to the wall should be kept. The unit should not be positioned near radiators or heat sources and direct insolation must be avoided.

In the event of insufficient air circulation or a too high ambient temperature pressure and temperature in the refrigerating system will increase.

The following connections are necessary at the site:

2.2 Mains Electricity

The voltage given on the name-plate must correspond to the local supply voltage.

CHRIST freeze dryers are units of safety class I and include a three-conductor connection cable and a shockproof plug.

2.3 Fuses on Site

The freeze dryer must be protected typically with a 16 A fuse.

2.4 Checking the Earth Connection

For checking the earth connection there is a screw for equalising the ground potential on the back panel of the freeze dryer. The check can be carried out by means of an appropriate measuring device.

2.5 Defrosting Water

The defrosting water is drained via the condensate drain valve on the left side of the unit. To drain the water place the hose supplied with the unit onto the nozzle. The defrosting water is collected in a vessel.

The defrosting water can also be drained directly via this hose. The defrosting water must be able to drain freely. To achieve this the hose must have a steady downward slope. It must be ensured that water does not collect in any part of the hose. The end of the hose always has to be above the level of the liquid in the vessel for the discharged defrosting water. Otherwise there is the risk of water and dirt residues being sucked into the condenser chamber if there is a vacuum when opening the condensate drain valve.

2.6 Vacuum Pump Exhaust

During the main drying phase the vacuum pump must be operated with open gas ballast valve. The oil mist which is produced must be removed.

A ½" hose is connected to the exhaust flange of the vacuum pump RZ-2 or RC-5 and a ¾" hose is connected to the exhaust flange of the vacuum pump DUO 005 or DUO 010. The hose either leads into the open air or into a vent.

During installation of the pipe care must be taken that condensate cannot flow back into the pump. With upward leading pipes it is safest to use a separator (Woulfe's bottle or wash bottle) in the pipe.

If draining of the oil mist should not possible we recommend that an exhaust filter (oil mist separator) is fitted. This filter prevents air pollution by oil mist which is emitted by the vacuum pump in smaller or larger quantities depending on the working pressure.

The filter is fastened to the exhaust flange of the vacuum pump.

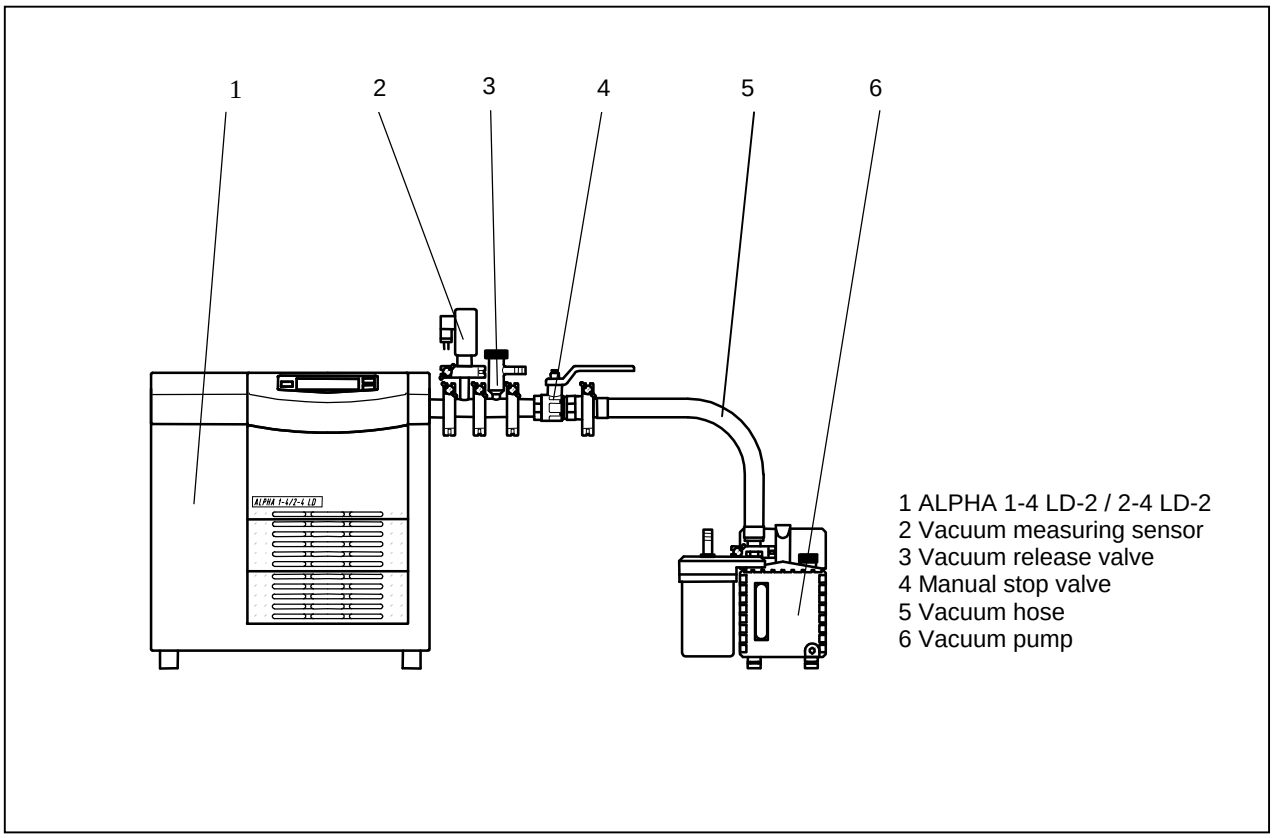
The filter is equipped with a pressure control valve which indicates the saturation of the filter. Cleaning or replacing of the filter insert must be carried out at the latest when the pressure control valve is activated. The collected oil is visible in the inspection glass and is drained via the discharging screw.

(Please refer to separate operating manual of the vacuum pump!)

2.7 Initial start-up

CAUTION! Ensure that the freeze dryer is correctly mounted and installed before initial start-up (see point 2.1 Site and following points).

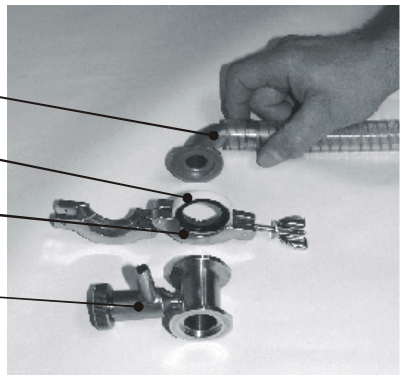
2.7.1 Connection of vacuum pump and installation of accessory components



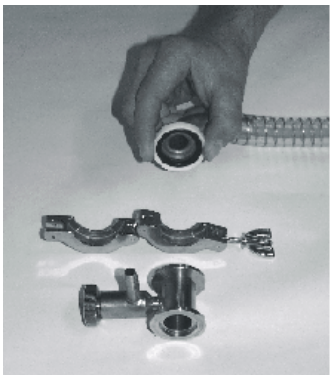
The accessory components are connected up to the freeze dryer **ALPHA 1-4 LD-2 / ALPHA 2-4 LD-2** according to the process flow diagram above. Centering rings and clamping flanges with wing nuts are used as connecting elements (small flange connections according to ISO 28403 respectively DIN 2861, see following instructions)

In addition the plug of the vacuum measuring sensor must be inserted into the socket “Vacuum measuring sensor” on the back of the unit (see point 3.4 connection of vacuum measuring sensor TPR 265).

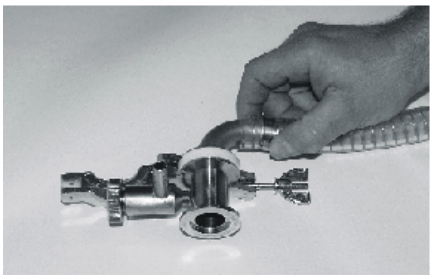
Instructions on connecting centering rings and clamping flanges



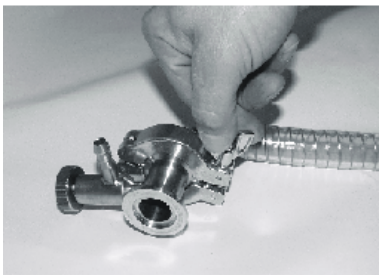
A Lay-out assembly of vacuum connections.



B Place centering ring on one side of small flange connection
(e. g. vacuum hose).



C Connect second flange (the centering ring must be positioned correctly!) and place clamping flange over the connection and press together.



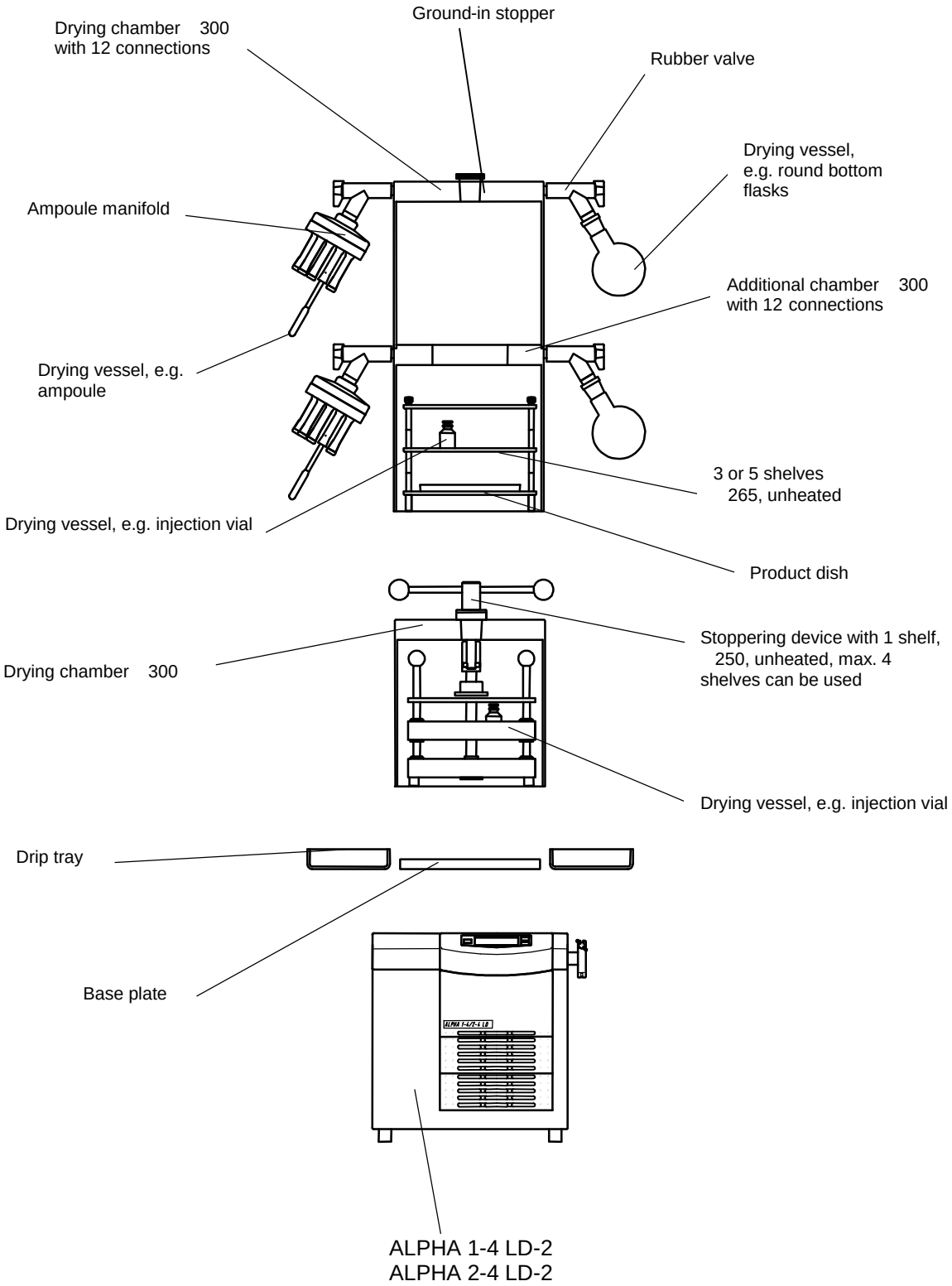
D Tighten the screw of the clamping flange by hand.

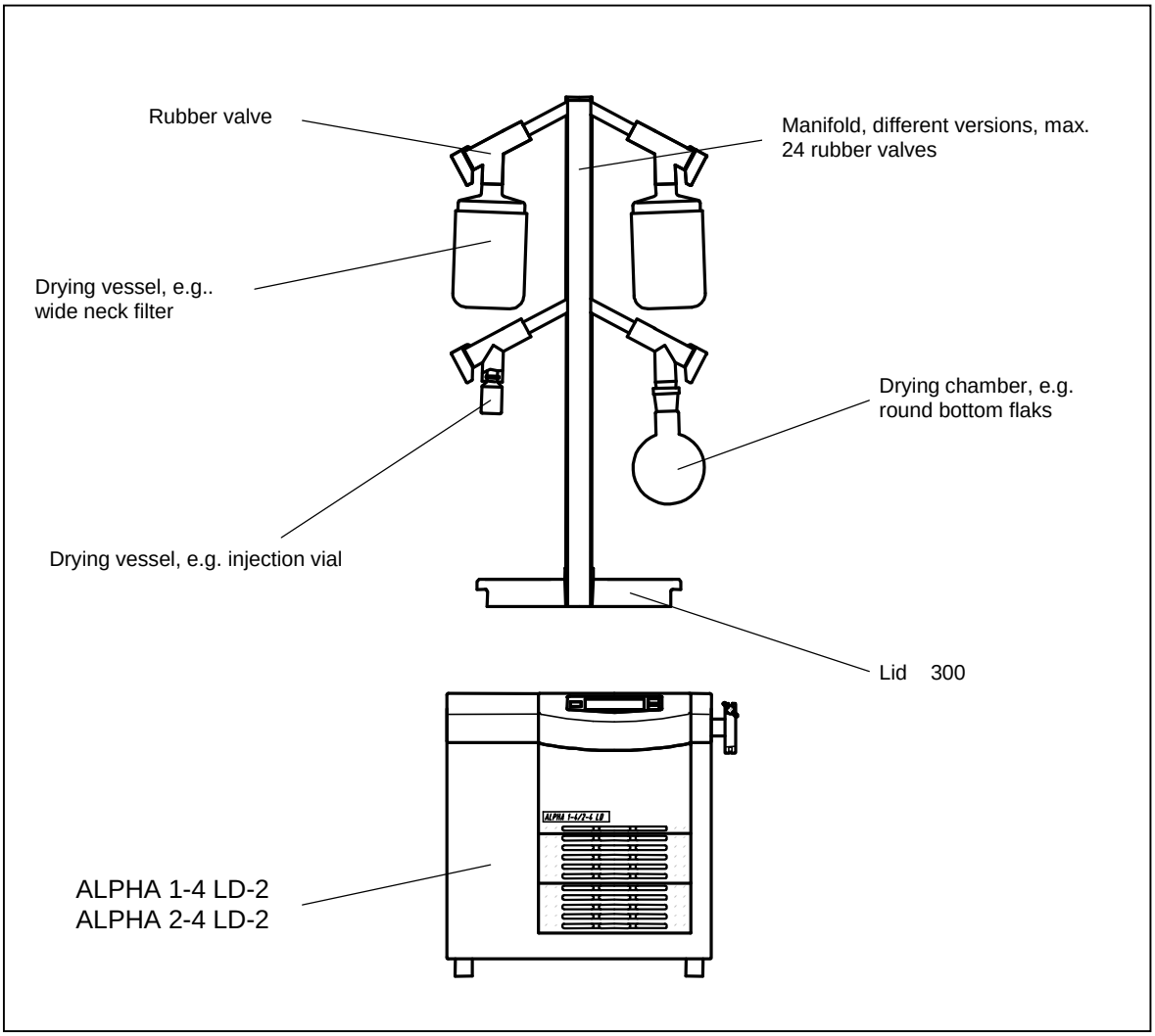
Other ordered accessories (e.g. drying chamber, shelves and connections for round bottom flasks) are added accordingly.

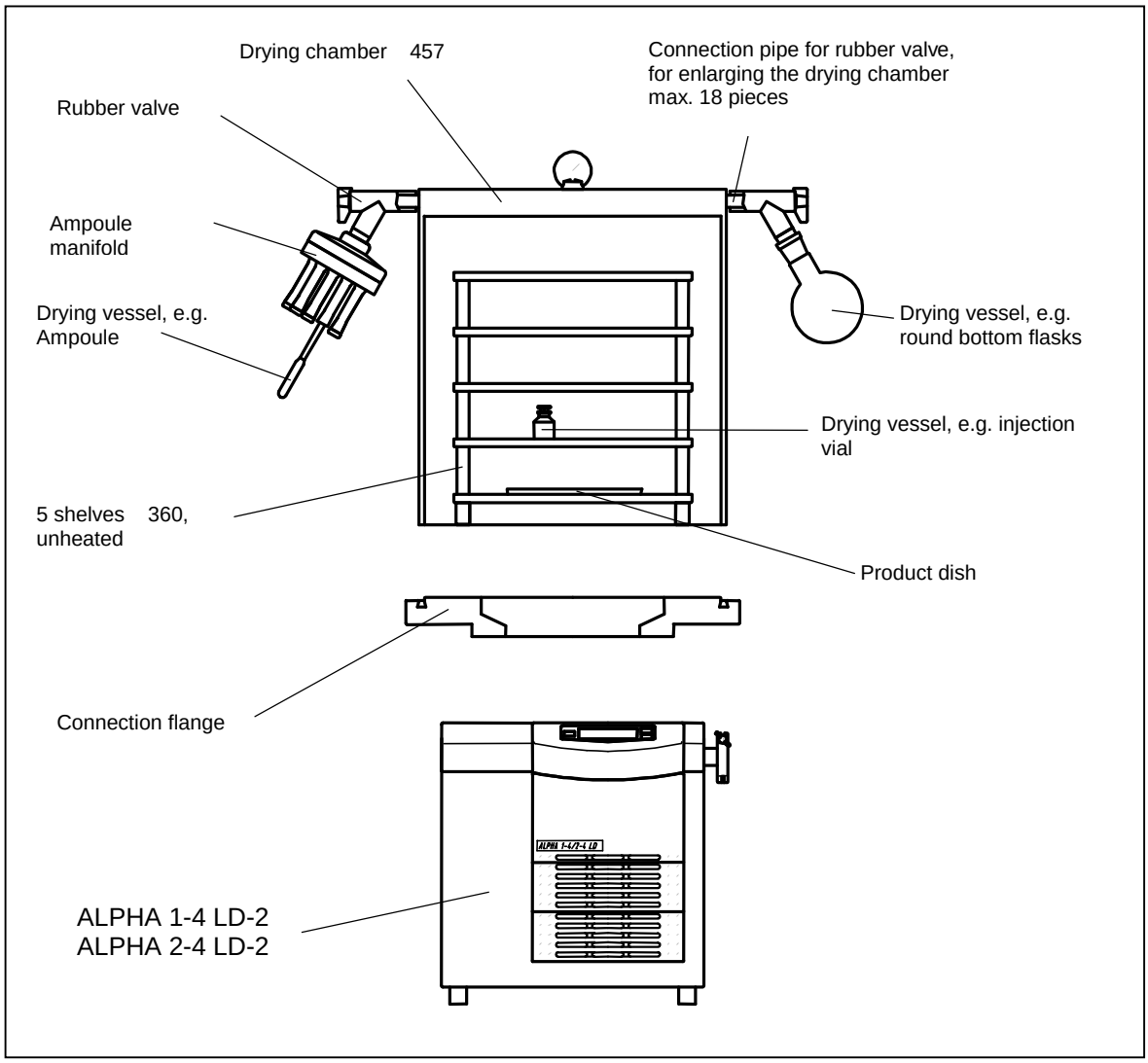
Example: Accessory for drying on 5 unheated shelves as well as individually sealable rubber valves for round bottom flasks.

Example: Accessory for drying on 2 unheated shelves with sealing device for injection vials.

Schematic diagram of accessories




Rubber valve
Manifold, different versions, max. 24 rubber valves
Drying vessel, e.g.. wide neck filter
Drying chamber, e.g. round bottom flaks
Drying vessel, e.g. injection vial
Lid 300
ALPHA 1-4 LD-2
ALPHA 2-4 LD-2


Drying chamber 457
Connection pipe for rubber valve, for enlarging the drying chamber max. 18 pieces
Rubber valve
Ampoule manifold
Drying vessel, e.g. Ampoule
Drying vessel, e.g. round bottom flasks
Drying vessel, e.g. injection vial
5 shelves 360, unheated
Product dish
Connection flange
ALPHA 1-4 LD-2
ALPHA 2-4 LD-2

2.7.2 Functional components and control elements

2.7.3 Preparing for Evacuation

The drying chamber made from acrylic glass with ground-in stoppers is placed on the ice condenser chamber.

The defrosting water valve at the left side of the unit and any rubber valves on the drying chamber are closed.

The vacuum pump is connected to the unit and to the mains.

2.7.4 Evacuation

The drying chamber is evacuated by switching on the vacuum pump.
After switching on the pump it must not be possible to lift the acrylic chamber or lid anymore.

2.8 Error messages

A possible error is showed in form of “ER : XX” (Error) in the lower part of the LC-Display. “XX” is marking the error code. In case of a fault, the display changes in one second intervals between error code and value display until the mains voltage is switched on and of.

All errors can be removed through the following measures:

- Switching on and of the mains voltage (mains switch; Power –On-Reset).
- Over the communication interface by using the command “reseterr”

Error number	Meaning, possible cause
ER10	Compressor 1 overpressure Compressor turns off (until overpressure is reducted)
ER 11	Compressor 2 overpressure Compressor turns off (until overpressure is reducted)

2.9 Error resolution

Error	Measure
Start of the instrument is not possible	
1. Mains failure	Mains plug connected?
	Check the fuse of the freeze dryer (Mains connection cord, fuse insert cord) respectively the fuse of the building and exchange if necessary
No display	
	Mains plug connected?
	Check the fuse of the freeze dryer (Mains connection cord, fuse insert cord) respectively the fuse of the building and exchange if necessary
Refrigeration system does not work	
No vacuum	
1. Position of the centering rings is not correct (Connection hose between vacuum pump and cooling trap)	Open small flange connection, insert Centering rings centrically, use vacuum grease if necessary
2. Lid seal not tight	Cleaning; call service if lid seal is damaged (Contact on page. 2)
3. Condensate drain valve defect (does not close)	Cleaning; exchange O-rings of the condensate drain valve

3 Control System LD-2

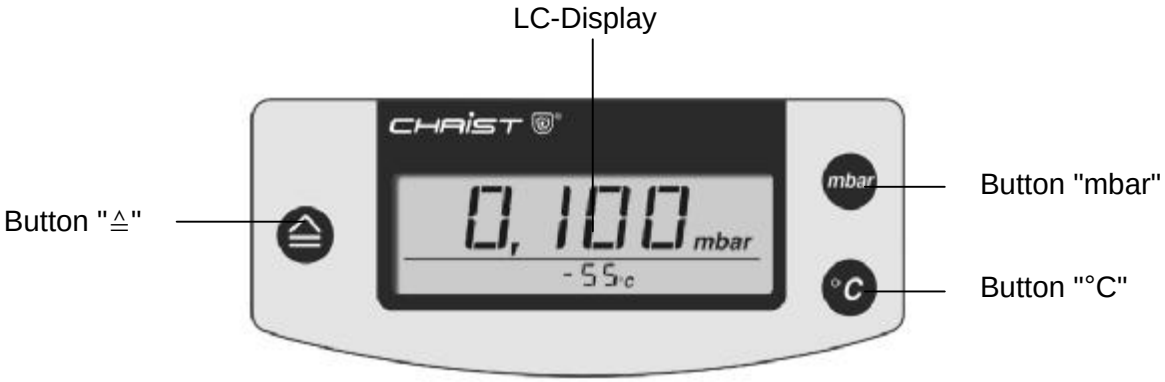
A particular advantage of the user friendly LD control system (Lyo-display) is that all functions are explained on the control panel.

- LC display showing the most important process data (temperature of ice condenser, vacuum)
- Conversion of temperature and vacuum in accordance with the vapour pressure curve above ice
- RS-232 communications interface (PC) is available as an option.

3.1 Mains Switch

The unit is switched on by means of the mains switch on the upper right side of the unit.

The LED-display lights up and the refrigerator is in operation.



3.2 "°C mbar" Button

On the freeze dryer **ALPHA 1-4 LD-2 / ALPHA 2-4 LD-2** the vacuum in the drying chamber or alternatively the ice condenser temperature can be displayed. The change-over is carried out by pressing the **"°C " or " mbar"** button.

The vacuum measuring sensor TPR 265 (accessory) is necessary for measuring the vacuum.

The upper pressure range - not important for freeze drying - is displayed in rough steps only (**"A"** corresponds to atmosphere).

If the unit is not equipped with a vacuum measuring sensor the display shows "----" at switch position "mbar".

3.3 "≙" Button

With this button the ice condenser temperature can be converted according to the vapour pressure curve above ice into the vacuum in the drying chamber or the measured vacuum can be converted into the temperature of the samples.

The possibility to convert the vapour pressure curve serves as orientation and helps to show the relation between pressure and temperature during freeze drying (see chapter 4).

3.4 Connection of the Vacuum Measuring Sensor TPR 265

Units without a vacuum measuring sensor can easily be retrofitted with the sensor **TPR 265** for measuring the vacuum. To do this the plug of the measuring sensor is inserted into the socket on the back of the unit.

The measuring sensor is supplied with a T-piece with small flange connections. With this T-piece the sensor is connected to the connection at the rear panel of the unit.

The vacuum measuring sensor must be adjusted If another value other than “A” (atmosphere) is displayed after switching on the unit (see point 6.6 “Adjustment of vacuum sensor TPR 265”).

4 General Information on Freeze Drying

Freeze drying is the most gentle process for drying biological and chemical products. It is based on the physical phenomenon of sublimation i.e. the direct conversion from solid to gaseous state. The frozen product is placed in the vacuum chamber for drying. The ice condenser can also be described as a vapour pump as the moisture which evaporates under vacuum during drying freezes onto the ice condenser. Consequently the vacuum pump is only intended to remove the air from the drying chamber (=gas pump) but not the vapour. In order to start the sublimation process, heat must be supplied to the product. This takes place during drying in round bottom flasks or wide-neck closed filter bottles etc. due to the much warmer environment (direct heat contact), on unheated shelves by means of heat radiation from the environment and directly by means of the shelves when heatable. Once the “free water” has been removed from the product, it is also possible to remove the crystalline bound water by means of very low vacuum. This part of the drying process is referred to as final drying (desorption).

Construction of the freeze dryer

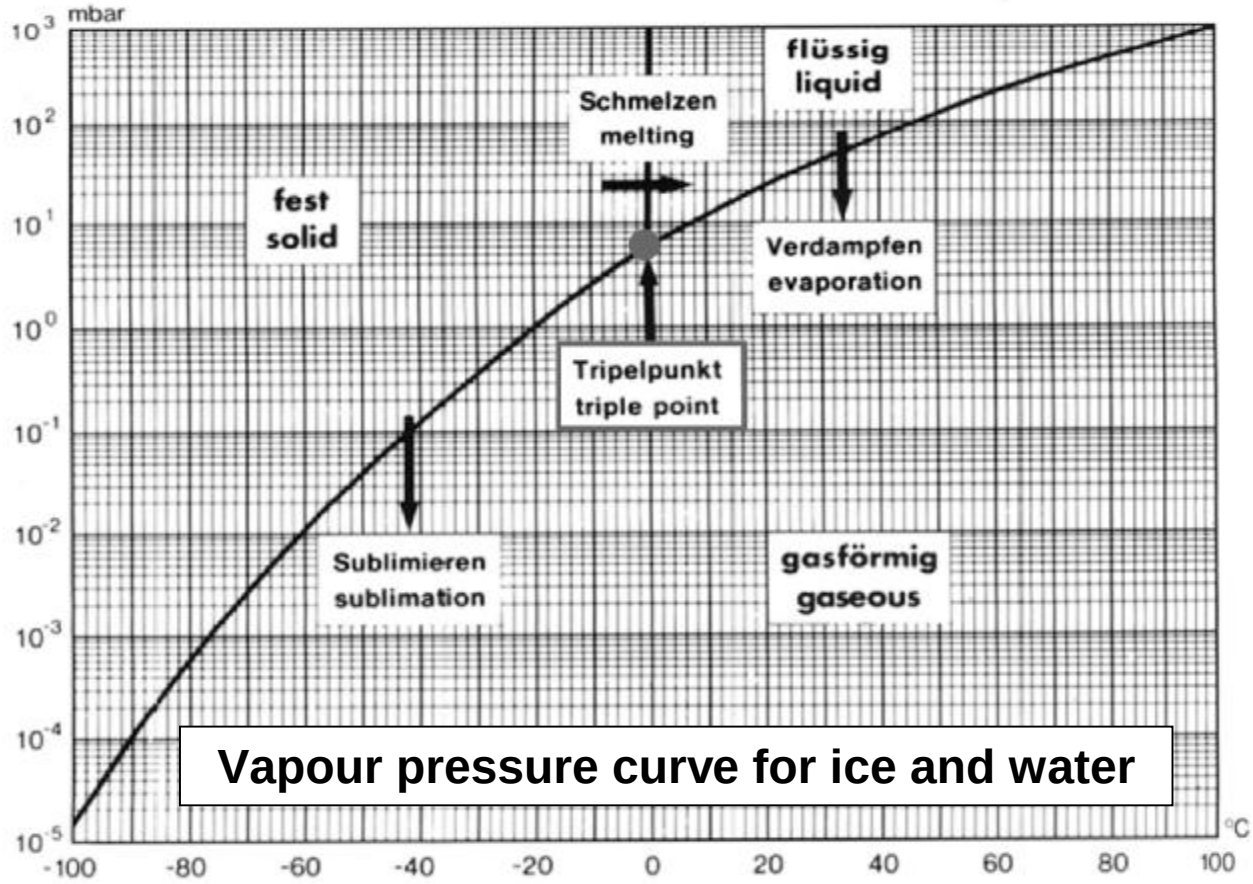
The components of a freeze dryer are :

- Drying chamber and heating accessories
  - a heatable and unheatable shelves for drying in dishes
  - b shelves with sealing device for drying in bottles
  - c rubber valves for connecting round bottom flasks, wide-neck filter bottles, etc.
  - d manifold for connecting round bottom flask, wide-neck filter bottles, etc.

- Pumps for air and water vapour
  - a vacuum pump to evacuate the drying chamber (= gas pump)
  - b ice condenser with temperatures from -50°C to -110°C (depending on type of unit) to condense the water vapour (= vapour pump).

Sublimation

The principle of sublimation is briefly explained using the phase diagram of water (freeze drying of mainly aqueous solutions, see vapour pressure curve).
If the atmospheric pressure is higher than 6.11 mbar, water passes through all three phases (solid, liquid, gas) when the temperature is lowered or raised. At 6.1 mbar the melting pressure curve, vapour pressure curve and sublimation pressure curve meet in one point, the triple point. At this point all three phases occur in parallel (simultaneously). Below this point, i.e. the vacuum is lower than 6.11 mbar, the ice is converted directly from a solid to a gaseous phase on reaching the sublimation pressure curve.



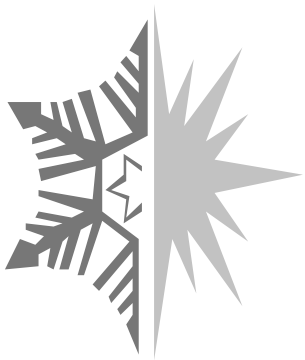
1mbar = 10²Pa

	= mbar	°C	= mbar	°C	= mbar	°C	= mbar
0	6,110	-20	1,030	-40	0,120	-60	0,011
-1	5,620	-21	0,940	-41	0,110	-61	0,009
-2	5,170	-22	0,850	-42	0,100	-62	0,008
-3	4,760	-23	0,770	-43	0,090	-63	0,007
-4	4,370	-24	0,700	-44	0,080	-64	0,006
-5	4,020	-25	0,630	-45	0,070	-65	0,0054
-6	3,690	-26	0,570	-46	0,060	-66	0,0047
-7	3,380	-27	0,520	-47	0,055	-67	0,0047
-8	3,010	-28	0,470	-48	0,050	-68	0,0035
-9	2,840	-29	0,420	-49	0,045	-69	0,0030
-10	2,560	-30	0,370	-50	0,040	-70	0,0026
-11	2,380	-31	0,340	-51	0,035	-71	0,0023
-12	2,170	-32	0,310	-52	0,030	-72	0,0019
-13	1,980	-33	0,280	-53	0,025	-73	0,0017
-14	1,810	-34	0,250	-54	0,024	-74	0,0014
-15	1,650	-35	0,220	-55	0,021	-75	0,0012
-16	1,510	-36	0,200	-56	0,018	-76	0,0010
-17	1,370	-37	0,180	-57	0,016	-77	
-18	1,250	-38	0,160	-58	0,014	-78	
-19	1,140	-39	0,140	-59	0,012	-79	

Conversion table " Vapour pressure above ice " (sublimation pressure curve)

The process steps of freeze drying

Prefreezing	+	Drying
under atmosphere pressure (e.g. at - 25°C)		under vacuum (e.g. at 0.1 mbar, equal to -42°C)
= formation of the ice structure		= keeps the water contents in the phase



Additionally necessary:

Energy input (= heat)

but: the material remains in the solid/ice phase!
(physical law: the vacuum is responsible
for the product-/steam temperature)

4.1 Freezing

The freezing of small quantities of product is carried out inside the ice condenser chamber of the **ALPHA 1-4 LD-2 / ALPHA 2-4 LD-2**. Larger quantities are pre-frozen in a deep-freeze.

If liquids are to be dried in bottles with a layer thickness of more than 1 cm we recommend that pre-freezing is carried out with a shell or spin-freezing-device in a cooling bath (see previous picture). Due to the centrifugal force the liquid to be frozen will rise on the wall of the bottle and freeze. With this freezing process the layer thickness is reduced and thus the total drying period is shortened considerably.

Freezing inside the unit is not necessary if the product is pre-frozen or stored in e. g. a deep-freeze. In this case, especially when freeze drying small quantities, it is advisable to pre-cool the shelves in order to avoid partial thawing during the evacuation.

Possible water residue must be removed from the ice condenser chamber. The defrosting water valve is closed.

The ground-in stopper of the acrylic chamber must be greased with high-vacuum grease!

The layer thickness of the product should not exceed 1 - 2 cm as otherwise this has a negative effect on the duration of the drying process.

4.2 Main Drying

The vacuum pump is switched on.

Please note:

Defrosting during the drying process is possible (visible foaming) when drying products containing e. g. solvents or high salt concentrations. In this case it is necessary to freeze the product as low as possible, e.g. in liquid nitrogen.

Warning:

Acidic products or products with a high solvent concentration cannot be dried without special protective measures and devices e.g. a cooling trap for protection of the vacuum pump (if necessary contact our company).

Special precautions are necessary when using azides because a dangerous explosive develops in combination with copper or non-ferrous metals! It is absolutely essential to consult our company!

As soon as sublimation of the water vapour from the frozen product begins, heat is extracted and consequently the product continues to cool down.

The maximum rate of sublimation is reached at the start of the drying process.

Depending on the rate of sublimation the ice condenser temperature and thus the pressure in the drying chamber respectively ice condenser chamber rises.

The duration of the main drying phase depends mainly on:

- the layer thickness of the product
- the solid content of the product
- the heat supplied to the product during the drying process
- the pressure inside the drying chamber during the drying process

With increasing pressure (not vacuum!) the rate of sublimation rises and the drying period is shortened.

The water vapour generated during the main drying phase is not pumped off by the vacuum pump but collected by the ice condenser.

The purpose of the vacuum pump is to lower the partial pressure of the non-condensable gases so that the water vapour can be transported from the product to the ice condenser.

However, small quantities of water vapour are also pumped off by the vacuum pump. Therefore, the vacuum pump is equipped with a gas ballast device.

If the gas ballast valve is open the extracted condensable vapours will be emitted via the exhaust pipe together with air.

For this reason the gas ballast valve must be open during the main drying phase!

The gas ballast valve can only be closed for final drying.

During the main drying phase the moisture is removed by sublimation, during final drying the bound moisture is removed by desorption.

This small quantity of water vapour generated during the final drying phase can be pumped off even when the gas ballast valve is closed (for several hours).

In general, operation with closed gas ballast valve is not necessary. The vacuum pump used reaches with open gas ballast valve a final pressure which corresponds to the water vapour partial pressure that can be reached.

The residual moisture of the dried product depends mainly on:

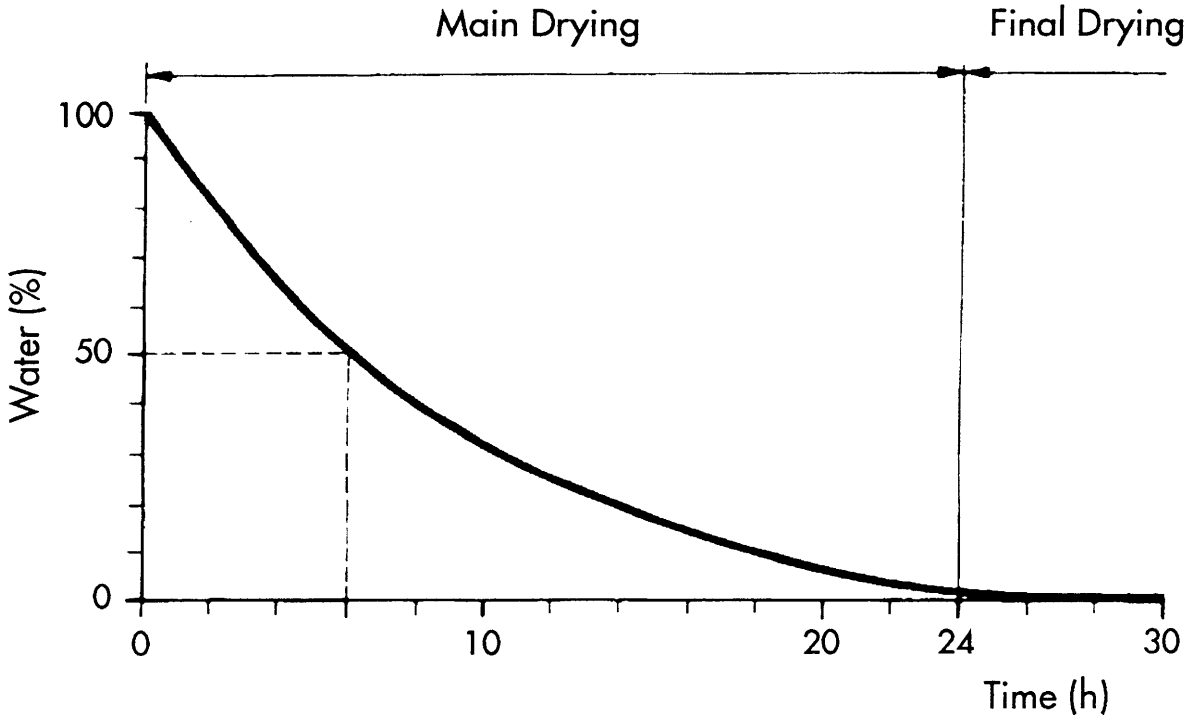
- the temperature of the dried product during the final drying process

- the final vacuum reached during the final drying process

The end of the main drying phase is reached, when the product temperature is nearly the same as the shelf temperature (temperature difference between shelf and product approx. 3°C to 5°C). If the crystalline bound water is to be removed from the product, the final drying phase can be started.

The following picture shows the drying process for a product containing approx. 10% solid matter. During the first quarter of the main drying phase 50 % of the water content is condensed. During the next quarter of the main drying phase 50 % of the remaining water content is condensed. This continues until the drying curve approaches the time axis asymptotically.

This typical drying curve is due to the fact that the area of sublimation recedes into the product and the water vapour still to be extracted has to pass through the already dried layers. During the drying process the inner resistance increases. Thus the drying curve is primarily determined by the latent heat of sublimation and the water vapour transport speed. In order to increase the specific heat conduction properties of the product to be dried and to keep the water vapour volume as low as possible it is necessary that drying takes place as close as possible to the eutectic point.



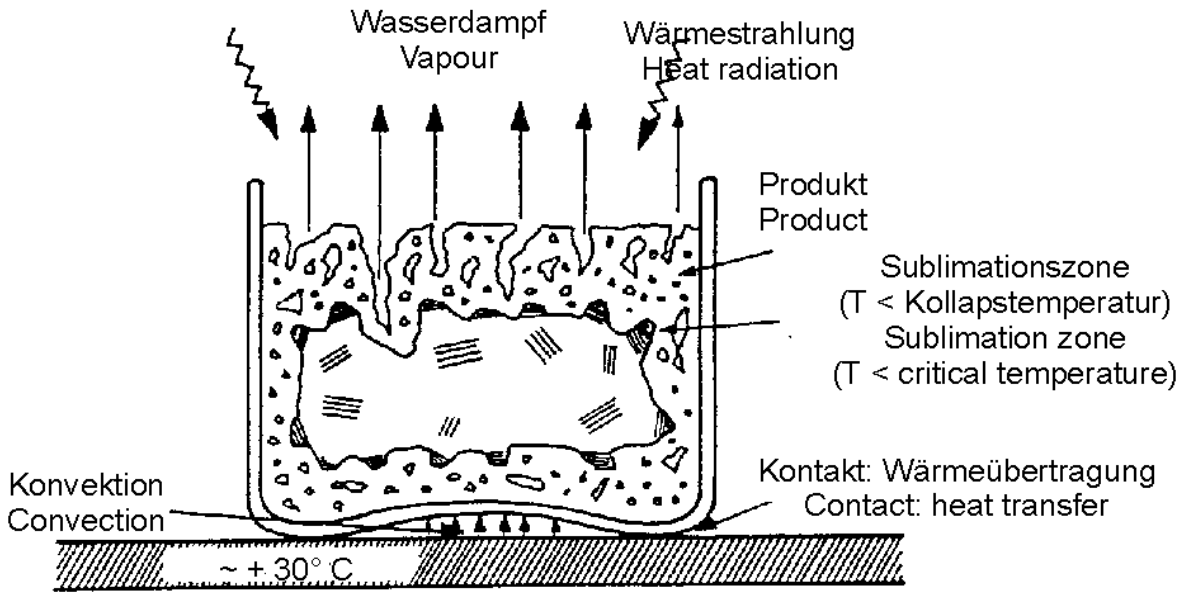
The drying time depends heavily on the drying vacuum. The nearer the vacuum is to the eutectic point in accordance with the vapour pressure curve above ice, the shorter the drying time is.

Interesting correlations:

1.0	gram of ice at		
1.0	mbar assumes a volume of	1	m³ vapour
0.1	mbar assumes a volume of	10	m³ vapour
0.01	mbar assumes a volume of	100	m³ vapour

Energy transport during drying

The required heat supply to the product to be dried takes place through direct heat contact in the drying chamber, heat conduction through gas or through radiation. Heat transfer by direct contact and heat conduction through gas are the most usual sources of heat in today's freeze dryers. The constraints caused by the former can be seen in the following diagram.



Effects of freeze drying of a product in a dish

Heat transfer takes place via the heated shelves[1], via direct contact with the bottom of the vessel and/or via the gas between the shelves and vessel by means of convection.

At the beginning of sublimation the transfer of heat is very effective from the wall of the vessel to the frozen product. However, soon an area develops which is ice free, porous and dried and has a corresponding temperature gradient between the wall of the vessel and the product. The poor heat conductivity of the already dried product can lead to an increase in temperature of the ice core. If the core temperature rises above the melting temperature, the product begins to thaw. This applies especially to inhomogeneous products and to great layer thicknesses. During this drying phase it is important to regulate the heat supply and control the temperature and pressure precisely.

[1] In so far as there are heated shelves, otherwise via radiation on the walls of the vessel or the exposed surface of the product

4.3 Final Drying

The final pressure in the drying chamber depends on the ice condenser temperature according to the vapour pressure curve above ice:

e. g. 1.030 mbar correspond to -20°C
0.370 mbar correspond to -30°C
0.120 mbar correspond to -40°C
0.040 mbar correspond to -50°C
0.011 mbar correspond to -60°C

The unit is in operating condition if the temperature of the ice condenser is lower than -50°C and the pressure is lower than 0.120 mbar.

The final pressure measured by the vacuum sensor when there is no product in the unit and its corresponding ice temperature value is mainly determined by the warmest place of the ice on the ice condenser chamber. Moreover, this value is affected by residues or parts of solvents in the product with a higher vapour pressure.

4.4 End of Drying and Venting

A rough indication of the end of drying is the vacuum and the ice condenser temperature. The ice condenser is no longer loaded and reaches the final temperature of approx. -50°C to -54°C. The pressure in the drying chamber decreases according to the ice condenser temperature.

The vacuum pump is switched off and the drying chamber is vented by a rubber valve or the defrosting water valve. A vacuum release valve for venting with nitrogen, another inert gas or air is available as accessory.

Then the unit is switched off and the product is removed.

4.5 Defrosting

Defrosting of the ice condenser is carried out at room temperature or with warm water. At a maximum the ice condenser chamber may be half filled with water.

During filling it is important that no water gets into the pipe connection for the vacuum pump and vacuum measuring sensor!

The defrosting water is drained through the defrosting water valve at the left side of the unit. To do this, a hose is put onto the nozzle. The defrosting water is collected in a vessel.

5 Description of the Freeze Drying Processes

5.1 Freezing Separately and Drying on Shelves

Possible water residue is removed from the ice condenser chamber. The defrosting water valve is opened and closed again so that the water residue can be drained. The ice condenser chamber should be wiped If necessary.

For pre-cooling the ice condenser the **ALPHA 1-4 LD-2 / ALPHA 2-4 LD-2** is switched on.

The rack is put onto the bottom plate. For smaller samples it is advisable to pre-cool the shelves in order to avoid a partial thawing during the evacuation process.

As soon as the shelves with the pre-frozen samples have been put in, the unit is sealed with the drying chamber and the vacuum pump is switched on.

5.2 Drying with Sealing Device

With the sealing device injection bottles can be sealed with ribbed rubber stoppers on one or two shelves under vacuum or inert gas. To do this the shelves are moved against each other by a pressure plate using a spindle.

The height of the pressure plate must be adjusted according to the height of the bottles. The screw for height adjustment is removed.

The threaded rod is screwed into the lower shelf until its slotted head is even with the black balls of the guide rod.

Then the pressure plate is fastened with the adjustment screw in such a way that it will rest on or slightly above the rubber stopper. When using two shelves the lower one as well as the pressure plate are put directly or immediately above the rubber stoppers.

Instead of the stopper the vacuum-tight rotary leadthrough is put into the standard ground socket of the acrylic chamber. Before inserting, the ground-in surface of the leadthrough is greased with vacuum grease.

After completion of the drying process the lever of the rotary leadthrough is turned to the right until a resistance is felt.

For the sealing of the bottles all shelves must be completely filled. For small quantities at least three spacers must be evenly put on each shelf (according to the height of the bottles with rubber stoppers).

The appropriate spacers are available on request.

5.3 Freezing Separately and Drying of Flasks

Possible water residue is removed from the ice condenser chamber. The defrosting water valve is opened and closed again so that the water residue can be drained. The ice condenser chamber should be wiped if necessary.

For pre-cooling the ice condenser the **ALPHA 1-4 LD-2 / ALPHA 2-4 LD-2** is switched on.

For drying outside of the ice condenser chamber different manifolds are available (see accessory catalogue). The drying chamber with 8 connections is mounted on the sealing ring on the bottom plate of the **ALPHA 1-4 LD-2 / ALPHA 2-4 LD-2**. Manifolds with standard ground joints NS 45/40 are connected via the ground-in socket of the acrylic chamber.

In order to ensure a vacuum-tight connection and to simplify removal of the manifolds the ground-in surface must be slightly greased with vacuum grease before use. The manifold is then put on and turned by 360° for even distribution of the grease.

Before the vacuum pump is switched on it is necessary to check that all valves are closed.

CAUTION! The frozen samples cannot be connected to the valves until a pressure of less than 1.030 mbar is reached.

Liquids are frozen in flasks according to the shell-freezing principle, manually or with a turning device. Due to this freezing process the layer thickness is reduced and the drying period is considerably shortened.

The rubber valves allow a continuous connection and removal of flasks during the drying process. Each rubber valve is equipped with a separation and venting device.

If the rubber valves are stiff they must be dismantled, cleaned, slightly greased with vacuum grease and reassembled.

Using a distributor a maximum of 15 ampoules can be simultaneously frozen in the cooling bath and connected to the manifold.

5.4 Freezing Separately and Drying of Ampoules Using a Manifold

The manifold is equipped with dummy plugs for connection of max. 48 ampoules so that it can be pre-evacuated.

The first hose is clamped in the middle with the supplied hose clamp and the blind plug is removed. The vacuum is preserved in the system.

The liquid in the ampoule is either frozen in a deep-freeze or under rotation in a cooling bath.

If shock-freezing is required we recommend that freezing is carried out in liquid nitrogen or in a cooling bath.

The ampoule is then connected to the hose and the hose clamp is removed. Thus the partial pressure in the ampoule is suddenly decreased and a partial thawing during the evacuation process is avoided.

With this procedure one ampoule after the other is connected.

Sealing of the ampoule is carried out in the same way. The hose of the ampoule to be sealed is clamped and the ampoule is sealed under vacuum using the blow lamp.

If the ampoule breaks during sealing the vacuum in the drying chamber is not affected due to the clamping with the hose clip.

The remaining glass from the ampoule is removed and the hose is closed with a dummy plug.

In this way one ampoule after the other can be sealed or new ampoules can be connected.

6 Maintenance

6.1 Vacuum Pump

For maintenance of the vacuum pump please refer to the enclosed instructions.

Additionally, we would like to emphasise the following points:

The oil level of the vacuum pump must be regularly checked using the inspection glass (in case of continuous operation at least once a week). Top up oil to the required level via the oil inlet. Due to the continuous operation with gas ballast oil consumption cannot be avoided. For topping-up see the instructions for the pump.

The first oil change must be carried out after approx. 100 operating hours. Subsequent oil change intervals depend on the operating conditions. In general, an oil change is necessary after approx. 500 to 1000 operating hours.

The oil change should always be carried out with warm pump.

6.2 Exhaust Filter

If the unit is equipped with an exhaust filter (necessary if the exhaust gases cannot be extracted into the open air or into a vent) take care that the condensate in the filter does not rise too high. The condensate is drained using a waste oil drain screw at the filter.

(Please refer to separate operating manual!)

6.3 Ice Condenser Chamber

Before each start-up ensure that all water residue has been removed from the ice condenser chamber. If necessary, wipe the ice condenser chamber.

We recommend that the defrosting water valve is opened and closed before each drying process.

6.4 Rubber Valves

Special attention must be paid to the rubber valves. If the valves are stiff, they must be dismantled, cleaned, slightly greased with vacuum grease and reassembled.

6.5 Condenser of Cooling Liquid

A laminated condenser for cooling liquid is used to cool the refrigerant compressed by the refrigerator. The condenser for cooling liquid is placed at the bottom of the unit. In intervals of a few months it must be checked for dust or dirt residues and cleaned if necessary. Cleaning of the heat exchanger can be carried out best by brushing, by using a vacuum cleaner from the outside or by using compressed air from inside the unit.

Excessive dirt on the condenser for cooling liquid leads to a decrease in performance and can lead to a failure of the unit!

Please note: The unit must not be turned upside down!

6.6 Adjustment of the Vacuum Measuring Sensor TPR 265

Adjustment of the vacuum measuring sensor should be carried out at least once a year if the unit is used continuously. Otherwise the operating point of the measuring sensor can change, e. g. "800 mbar" is indicated instead of "A" (atmosphere).

For adjustment of the sensor, two values must be set:

"A" = Atmosphere
"HV" = High-vacuum

The high-vacuum range of the sensor is more stable so that a adjustment is in most cases only necessary for atmosphere.

"A" Adjustment:

- Insert the plug of the sensor TPR 265 into the socket at the rear panel of **ALPHA 1-4 LD-2 / ALPHA 2-4 LD-2**, switch on the unit and preselect the vacuum display.

- Switch on the vacuum pump and let it warm up for approx. 15 minutes.

- Mount the TPR 265 on the vacuum connection piece of the vacuum pump.

- Switch on the vacuum pump and evacuate for approx. 3 minutes, then vent the unit slowly.

- Wait for approx. 10 minutes. For the adjustment of the atmospheric value it is important that the TPR 265 must be in exactly the same place as it will be used in later!

- Press the conversion button "=" of **ALPHA 1-4 LD-2 / ALPHA 2-4 LD-2** and set the transition point in the display from "A-FF" to "A-or" (i. e. between "FF" and "Overrange") using the potentiometer "ATM" of the TPR 265.

"HV" Adjustment:

The high-vacuum adjustment must be carried out with a two-stage slide vane rotary vacuum pump in good working order:

- Mount the TPR 265 on the vacuum pump and evacuate for approx. 10 minutes.

- Set the transition point in the vacuum display of **ALPHA 1-4 LD-2 / ALPHA 2-4 LD-2** between 0.0026 mbar and 0.0030 mbar using the potentiometer "HV" of the TPR 265.

Vent the unit slowly and carry out the adjustment process once again.

If problems arise during the adjustment process of the vacuum measuring sensor, the vacuum sensor must be sent to Christ to be checked. The vacuum measuring sensor has a limited life time. Defective sensors are exchanged.

6.7 Cleaning

6.7.1 Cleaning of the Freeze Dryer

Use soap water or other water-soluble, mild agents for cleaning of the freeze dryer. Avoid corrosive and aggressive substances. Do not use alkaline solutions or solvents or agents with abrasive particles. Remove product residues from the chamber using a cloth. It is recommended that the lid to the freeze dryer is left open when the freeze dryer is not in use so that moisture can evaporate. **If there is the risk of toxic, radioactive or pathogenic contamination, special safety measures must be considered and adhered to.**

6.7.2 Cleaning of Accessories

When looking after accessories special safety measures must be considered as these are measures to ensure operational safety and reliability.

Chemical reactions as well as stress corrosion cracking (combination of changing pressure and chemical reaction) can affect or destroy the structure of the metals and plastic parts. Hardly detectable cracks on the surface expand and weaken the material without visible signs. When visible damage of the surface, a crack, a mark or any other change, as well as corrosion is detected, the part in question (shelf, vessel, drying chamber etc.) must be replaced immediately for safety reasons.

Fans, lid seal, vessels, racks, acrylic chamber and shelves must be cleaned regularly In order to avoid damage.

Cleaning of accessories should be carried out away from the freeze dryer once a week or preferably after every use. **If there is the risk of toxic, radioactive or pathogenic contamination, special safety measures must be considered and adhered to.**

Aluminium accessories are particularly subject to corrosion. A neutral agent with a pH-value between 6 and 8 should be used for such parts. Alkaline agents (pH > 8) must be avoided. Thus life time is increased and corrosion is reduced considerably.

Careful maintenance through the user increases life time and avoids premature failure of accessories. Damage caused by insufficient care does not constitute a warranty claim.

6.7.3 Maintenance of the Condensate Drain Valve

Special attention must be paid to the condensate drain valve. If residues from previous drying processes deposit on it, there is the risk of faulty operation of the freeze dryer. Therefore, take care that no product or other residues will get into the pipe to the condensate drain valve.

6.7.4 Disinfection of Chamber and Accessories

All usual disinfectants like e. g. INCIDUR, Melisiptol, Sagrotan, Buraton or Terralin (available at laboratory retail suppliers) can be used.

NOTE! Check compatibility with lid; also see enclosure “Chemical properties of PLEXIGLAS (acrylic glass).

The freeze dryers and the accessories consist of different materials. A possible incompatibility must be considered. For autoclaving the temperature stability of the individual material must be checked. Please consult us if in doubt. **If dangerous materials are used, the freeze dryer and the accessories must be disinfected.**

6.7.5 Checks by Operator

The operator has to ensure that the important parts of the freeze dryer relevant for safety are not damaged.

This especially refers to:

1. Acrylic lid or acrylic chamber
2. Seals
3. Oil level of vacuum pump
4. Accessories, especially changes like corrosion, cracks, wear and tear of material etc.

Furthermore, an earth conductor check must be carried out regularly.

7 Error Correction

7.1 Power Failure

In the event of a power failure during the drying process the batch may become unusable. Whether the batch can be saved depends on the drying phase in which the product was when the power failure occurred.

It is important to distinguish between the main drying and final drying phase:

The product is in the final drying phase when the residual moisture has reached approx. 5 %. Below this value the product is generally not damaged in the event of a power failure.

If the product is in the main drying phase we recommend that the unit is vented, the product taken out and stored in a deep-freeze. Before further operation the defrosted condensate must be drained.

7.2 Insufficient Vacuum

Special attention must be paid to the high-vacuum valves. The defrosting water valve as well as the rubber valves must be checked.

We recommend that after disconnecting the mains plug the left side panel of the unit is unscrewed and then the hose inside the unit is detached from the defrosting water valve, the pipe connection is sealed with a rubber stopper, and the unit evacuated. If the unit will now reach the necessary operating pressure there is a leakage in the valve. This is caused by residues from the drying process, fluff from cleaning cloths or wear and tear of the O-rings of the valves.

To eliminate this fault we recommend that the unit is evacuated and vented by means of the defrosting water valve so that any residue is removed. If necessary, the O-rings must be replaced.

The next step is to check all the small flange connections between the freeze dryer and the vacuum pump and especially the position of the centering rings. It is usually not necessary to grease the sealing rings with high vacuum grease. If so, then use very little!

If the leakage cannot be eliminated in this way, the manual valve must be cleaned or replaced.

Check the oil level in the vacuum pump, change oil if dirty, carry out pressure test.

Check if the whole surface of the ground-in socket of the acrylic chamber has been greased evenly with vacuum grease.

When using drying chambers with 8 connections for rubber valves the valves should be taken off and the connections should be sealed with rubber stoppers. To check the valves they are connected one after the other and tested under vacuum.

Check the vacuum measuring sensor for pollution such as water residue.

The vacuum measuring sensor has a limited life time due to its design principle. Vacuum sensors are available as a spare part (order no. 125479).

Check the vacuum display with a suitable testing unit (if available).

In order to locate a possible leak we recommend that the vacuum measuring sensor is directly connected to the vacuum flange of the vacuum pump. If the warm vacuum pump reaches a final pressure of at least 0.011 mbar, the vacuum pump and the measuring system can be presumed to be in working order. There is probably a leak in the unit if insufficient vacuum is not caused by an insufficient ice condenser temperature.

The vacuum pump does not switch on:

The vacuum pump is equipped with a protective switch for the drive motor.

(Please refer to separate operating manual.)

General information:

The vacuum checks should be carried out when the ice condenser is at a low temperature.

7.3 Unit does not function

If the refrigerator does not work and the temperature or the vacuum is not displayed after operating the mains switch, the following must be checked:

- Is the mains switch plugged in?

- Check the fuses F1 and F2 (draw in the power supply plug on the back of the unit).

7.4 Insufficient Ice Condenser Temperature

The refrigerator is equipped with thermal motor protection. In case of excess ambient temperatures or overload the protection device is released and the refrigerator is switched off.

Once the permissible operating conditions are reached again (after a few minutes), the refrigerator is automatically switched on again via the motor protection switch.

The minimum ice condenser temperature of approx. -54°C is reached if the ice condenser is not loaded and the ice condenser chamber is evacuated. Sufficient air circulation is necessary.

M A R T I N C H R I S T

Gefriertrocknungsanlagen GmbH

Legends referring to the following drawings ALPHA 1-4 LD und ALPHA 2-4 LD

"Refrigeration System **ALPHA 1-4 LD/LSC**" Drawing no. 170131
"Refrigeration System **ALPHA 2-4 LD/LSC**" Drawing no. 170132

Nr.:	**Description:**
004	Overpressure switch refrigerator 1
005	Refrigerating compressor 1
007	Fan for compressor
008	Condenser
010	Collector/Dryer
013	Heat exchanger
014	Capillary tube
019	Schrader valve suction side of compressor
020	Schraderventil
023	Overpressure switch compressor 2
024	Compressor 2
033	Capillary tube ice condensor
038	Schrader valve suction side of compressor 2
039	Schrader valve
071	Ice condenser chamber
072	Ice condenser
080	Condensate drain valve
083	Gas ballast valve (installed in vacuum pump)
089	Connection vacuum pump
090	Connection condensate drain
095	Time relais for 2. stage of compressor
097	Mains input 230 V 50 Hz
099	External ground connection
150	Mains switch
151	Control System **LD-2**
160	Main fuse 230 V 10 A

Declaration of Contamination

Of Freeze Dryers, Vacuum-Concentrators, Centrifuges, Accessories and Vacuum Pumps.

This declaration may only be filled in and signed by authorised staff.

Repair Order dtd. : _____

Order No. : _____

Type of unit : _____ Serial No. : _____

Type of unit : _____ Serial No. : _____

Type of unit : _____ Serial No. : _____

Type of unit : _____ Serial No. : _____

Accessories : _____

_____

Is the equipment free from harmful substances ? YES **O** NO **O**

If not, which substances have come into contact with the equipment?

Name of the substances : _____

_____

Remarks (e.g. to be touched with gloves only) :

General characteristics of the substances :

Corrosive	**O**	Explosive	**O**
Biologically hazardous	**O**	Radioactive	**O**
Toxic	**O**		

Which combination of substances may lead to the development of hazardous materials?

Name of the substances : _____

_____

Has the equipment been cleaned before shipment? YES **O** NO **O**

Is the equipment decontaminated and therefore does not pose a health risk? YES **O** NO **O**

Prior to repair, radioactively contaminated components must be decontaminated according to the valid regulations for radiation protection.

Legally Binding Declaration

I / we hereby declare that the information on this declaration is correct and complete.

Company / Institute : _____

Street : _____

Postcode, City : _____

Tel. : _____ FAX : _____

Name : _____

Date : _____ Stamp :

Signature : _____ _____

Return Declaration

Following declarations are for the health and safety of our employees. Fill in the forms and attach them when returning freeze dryers, centrifuges, spare parts and accessories. Please understand that we cannot carry out any work before we have the declarations. (We recommend that you make several copies of this page.)

!!!! IMPORTANT – This form must be glued onto the outside of the packaging !!!!

Return Declaration

	YES	NO
Decontamination declaration inside :		
Unit / component contaminated :		
Unit / component unused (new) :		

!!!! IMPORTANT – This form must be glued onto the outside of the packaging !!!!